PATHOLOGY OF PHTHISIS PULMONALIS.

Mr. President, Ladies and Gentlemen :—I must first say that when I left home last evening I was not aware of what was before me; I have not come prepared to make a set speech this evening, and if you find what I say rather disconnected, I hope you will excuse me.

What I want to say in connection with this subject is on the part of the pathology and etiology of the disease, and how we have arrived at the place we now are, in which we consider we have done something towards curing the disease called consumption; I use the word consumption in the generic sense as applied to those diseases that are found associated with consolidation and decay of the lungs, together with wasting and emaciation of the body. We know that in making a post-mortem examination of a case of disease of the lungs we find a variety of changes there, appearances indicating in some cases that the disease has not progressed very far, while in others we find large consolidations, and in some parts large cavities caused by breaking down of this consolidation. So far we have only seen, with the naked eye, one appearance which is constant, and that is consolidation. Now if we stop

there, at the naked eye appearance, we have simply one form of disease, consolidation of the lung with breaking down afterwards and formation of cavities; but when we bring in the aid of the microscope, and prepare sections cut from the lungs, we find a totally different state of things. I think this is one of the most important problems that we have before us at the present time, that is to say, whether we are to believe in the unity or duality of this disease. We know that the unity of this disease has been taught by a large number of men who fully believed in it, but I have been working on this subject for a number of years, and I simply cannot satisfy myself that it is so. I would point out that if you take those cases where there is consolidation of the lungs, and carefully harden those lungs, cut sections from them, stain and prepare them for the microscope, and examine them, you will find that they divide themselves into two kinds. You will find that the one is inflammatory, and the other a new growth in the lungs, which is tubercle. I have taken these photographs from cases of acute miliary tuberculosis, in which you can see the process in the early stage, and I think they will show you the distinction. It seems to me that at the present time it is an important question as to whether there are two distinct diseases or not. You are aware that some dogmatic writers have insisted upon the unity of phthisis, but I have no hesitation in saying, from a careful study of diseases of the lungs, that this is not the case. There are two distinct forms of disease in the lungs, one the inflammatory breaking down, the other a new growth. I would therefore as a basis, divide lung diseases into two kinds, the inflammatory and the tubercular. And I would then, as a kind of sub-class to

these, add acute miliary tuberculosis, which must be distinguished from these because its symptoms are so different; it does not run a long course. It never causes ulceration into the respiratory passages, and in cases of acute miliary tuberculosis you never get bacilli in the sputum, therefore I would make a sub-class of this. Take the inflammatory form of phthisis; we all know the form of pulmonic phthisis where you have in the first place a catarrhal pneumonia, there may be bronchitis, and extension of that into the lungs and an inflammatory condition of the lungs which ends in consolidation there. This consolidation may clear up and leave the lungs as whole as they were before, provided the damage done by the inflammatory process has not been so great as to destroy the vitality of that part of the lungs affected; but if, on the other hand, consolidation has gone on and the flow of blood through the parts has been arrested by the inflammatory process, and the damage to the lung is so great that a part of it is destroyed, that is dead, we then have retrograde changes resulting in what we call caseation. There is then the inflammatory form; this, if carried out to the destruction of the parts, ends in caseation and liquefaction, which ejected through the bronchi leaves a cavity in the lung. That seems to me perfectly clear; I think that is the experience of all of us.

In the case of tuberculosis we have a totally different thing, we have there the formation of tubercles. Now I must explain what I mean by tubercles. It is a new growth in the lungs composed of a fibroid tissue; I call it fibroid tissue because I am not clear that it is fibrous tissue. The reaction is exactly the same as that found in fibrous tissue; it is distinctly a new formation in the lungs, and it is not of an inflammatory

character, it contains one or more giant cells. This is distinctly a new formation; in a well-stained specimen it looks something like an elastic tissue, but I do not think it is ordinary fibrous tissue. There is this peculiarity in regard to tuberculosis, you do not get a large tubercle, when you first see the consolidation it is not one single tubercle, but an aggregation of small tubercles. A tuberculosis grows in the lungs by beginning as one or two small ones together, which gradually increase in size, and numerous smaller ones are formed around the edges, so you get a large mass which looks like a consolidated form of pneumonic phthisis. This tissue is peculiar, it has this characteristic that it readily breaks down, and for this reason it has been included in the infective class, together with the lesions of syphilis. Now we know there is a kind of tissue formed in syphilis which varies very much, but still it is a new growth, and we know that under certain drugs this can be changed and destroyed and broken down, leaving nothing behind but destroyed tissue. In tuberculosis we also have a new tissue, but of a more stable character. We know that in small tubercles, after they have grown to a certain size, the centre indicates the beginning of necrosis, and on the outside we have the reticular tissue containing the giant cell. The next stage is that the whole or a part begins to break down, and then it passes into what we call caseation, because we do not know any better name. The chemists, who ought to be able to support us in this, never do so; we have not yet had the composition of caseous matter worked out. What I want to know is whether the caseation in phthisis is the same as that of the breaking down of tuberculosis. If that was shown we would

have more data to go on in forming an idea of the disease than at present. In these two forms we have consolidation as one cause of inflammation, and in the other a new growth, both resulting in breaking down and the formation of what we may call caseation. The result of these two diseases is the same, that is to say, formation of cavities in the lungs, while the beginning is totally different.

Before I speak of the formation of tubercles in the lungs I would pass on to acute miliary tuberculosis. Every case of acute miliary tuberculosis that I have been able to get during the last nine years I have examined carefully, and have found always the same results. I have had to place them in two classes, the inflammatory and the tubercular. So we have acute miliary tuberculosis differing so much from either chronic phthisis or the more chronic form of pulmonary disease, still being the same clinically; it is almost impossible at present to discriminate between the two forms of acute miliary tuberculosis. In post-mortem examination of the lungs you cannot tell them apart, yet when we study these small nodules in the lungs we find two kinds, the inflammatory and the tubercular, and in this condition we can study them perfectly. But this is the difficulty we have to contend with in studying the disease and the lesions produced by that disease; we cannot get at the initiation of the disease in the ordinary forms, but we can in acute miliary tuberculosis. Figs. 1 and 2 are photographs of cases of children that died of acute miliary tuberculosis. The disease lasted about the same time, and the children were of the same age, the physical signs and symptoms were alike and were diagnosed as miliary tuberculosis. As far as I have gone, and I am certainly within bounds in

saying that I have cut over a thousand sections of these lungs, and stained and examined them, I have never found any section made from either one of these lungs that did not absolutely put itself into one class or the other, inflammatory or tuberculous. So also in the more chronic form the division is absolute between the two, you

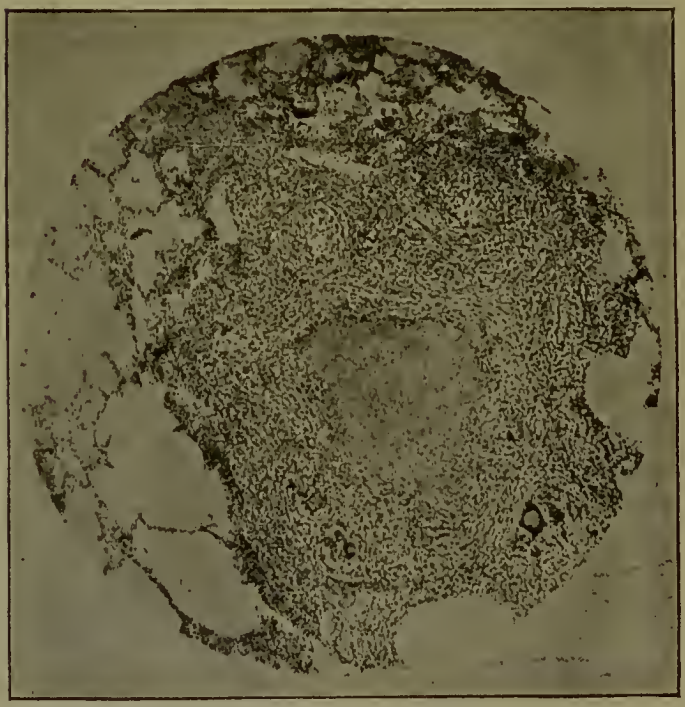

FIG. 1.—Typical reticular tubercle (essential type of tuberculosis; Payne). Fibroid tissue, giant cells, necrosed centre. From a case of pulmonary tuberculosis where all the lesions were of this structure, and no tubercle bacilli could be found.

may divide the disease absolutely into two classes, tubercular and inflammatory.

With regard to the tubercle, I may say this:

It has been said that the reason why there is this difference of opinion between some observers is that some take one form of tubercle and some another, on which to form their basis as to what a tubercle is. That is utterly wrong; you may

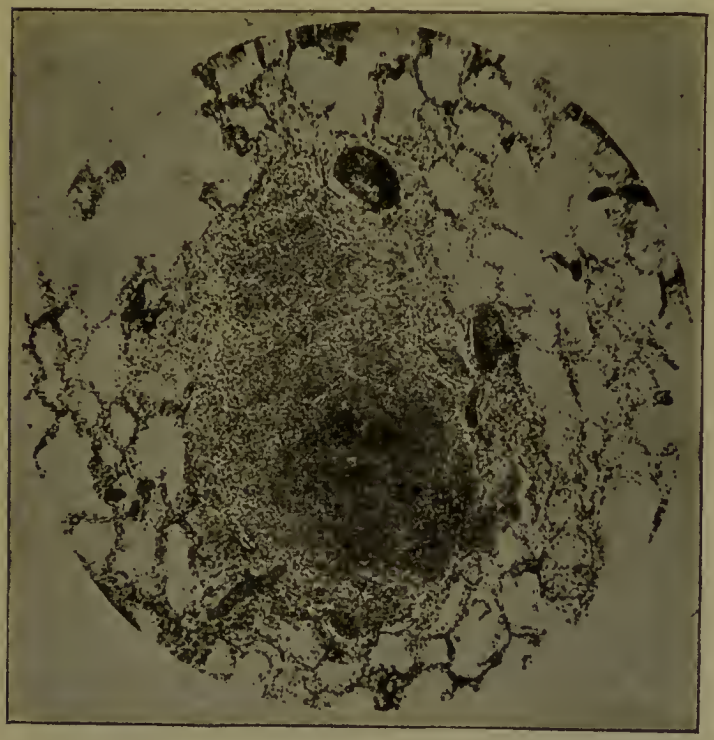

FIG. 2.—Caseous tubercle in lung of child in case of acute miliary tuberculosis (so-called). Centre of mass contains a large number of tubercle bacilli.

make fifty or one hundred or more sections of the lungs in cases of acute miliary tuberculosis of the tubercular kind, and you will never find two that are exactly alike. There is always this sharp difference between the two forms: you have on

one side an inflammatory process, with no attempt at structural formation; in the other there is a reticular structure, a new growth. Now, coming to the initiation of these two, and finding out the earliest stages in their growth, and finding that these two begin in the one form inflammatory

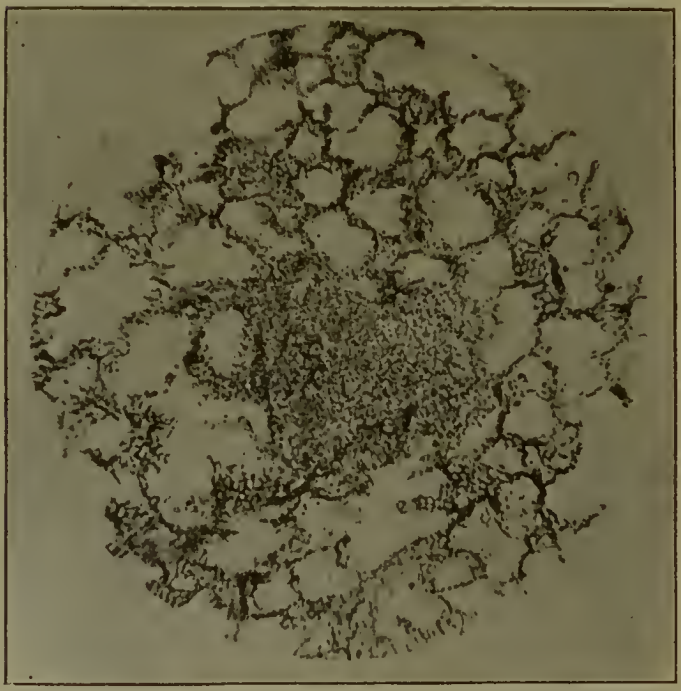

FIG. 3.—Inflammatory tubercle commencing. Lung of child. Case diagnosed as acute miliary tuberculosis. Lung injected with Berlin blue.

from the commencement, and in the other reticular, we are justified in deciding that these must be two distinct diseases, this the inflammatory condition, and that the tubercular. (Figs. 3 and 4.) This photograph shows that the commence-

ment of the one is reticular from the beginning; you may see where a small tubercle is commencing, and you see this is formed from a new growth, and that is to be found in the very commencement; while the other is nothing but a collection of inflammatory cells. I have said enough to show that these are two diseases.

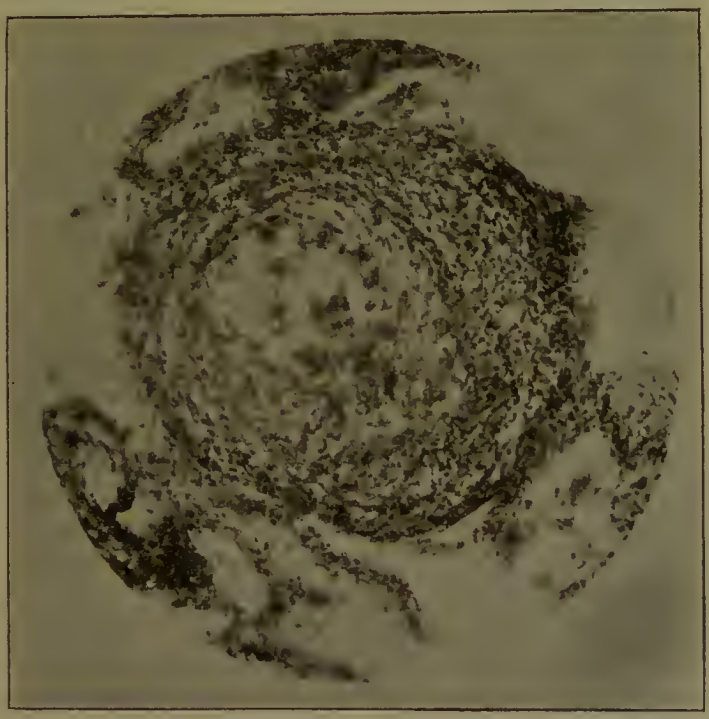

FIG. 4.—Reticular tubercle commencing, from a case of acute miliary tuberculosis.

Unfortunately, I am not on the fashionable side, and what I have done on this subject is ignored; but I think we have come to a time when we cannot afford to ignore this. This is a more

highly magnified specimen, showing the tubercular structure, with large giant cells in it.

Now, in regard to the etiology of these two diseases; it seems to me that there ought to be no difficulty in working out the etiology of the inflammatory form of phthisis; it begins in inflammation and ends in the ordinary way; it simply breaks down. But the tendency is to consider what was formerly called causative as now only predisposition, that leads one only into difficulty, because now we have to face the question of the relationship of the tubercle bacillus to this process. Coming to the earliest stage of the disease as shown in these two photographs, we are told by many observers of the present time, that the tubercle bacillus is the virus of the disease. That phthisis pulmonalis and tuberculosis are one and the same disease; that wherever the tubercle bacillus is found, there is tuberculosis. Therefore, if we want to find the starting point, we must examine the earliest stage of the disease; but when we look at the very commencement of these two forms and look for the tubercle bacillus, what is the result? We cannot find it. I can say that in all the cases I have examined I have never been able to find the tubercle bacillus at the commencement of the process in the human lung. I have carefully picked out from the earliest cases what seemed to be representative ones, and photographed them, so that you can see what is there. This is the commencement of the disease, and the virus of the disease, the thing which starts it, is absent. There is another little difficulty in connection with it; that is, in these two forms in acute miliary tuberculosis you will never find the tubercle bacilli in the sputum. But you will never examine one of the inflammatory type of that disease without finding in the centre of the

inflammatory mass a large number of tubercle bacilli. Hamilton has described this peculiar form very well; he calls it "disseminated catarrhal pneumonia;" and he says that not a few cases recover from this. He says that in this form you will find no trace of tubercular formation, no organization, no structure whatever. That agrees exactly with what I call the inflammatory form of acute miliary tuberculosis, and you will see in these specimens that the centre of the inflammatory mass contains a large number of tubercle bacilli. In the tubercular form I have examined many cases where there were no tubercle bacilli at all to be found, not only at the commencement of the disease, but all the way through it. There were none to be found in many hundred sections I had made of that condition; and others have put it on record that they had been unable to find them. Further than that, I have had cases of tuberculosis in the more chronic form, where the disease existed for a long time, under observation, and where there were no bacilli in the sputum; where the post-mortem examination showed large cavities in the lungs, and sections of the lungs showed large tubercle breaking down and forming cavities, but without one single bacillus in them. So if the tubercle bacillus is the virus of the disease, as far as I can see, it is absent from the commencement of the process in both forms; and even absent throughout the whole course of the disease in some of these forms of tuberculosis.

The next thing which is supposed to show the tubercle bacillus in its position, is the effect when inoculated in animals. It has been stated positively, and on this is founded a great deal of what has been laid down dogmatically, that the lesion produced by inoculating tubercular material is identical with the small tubercle you find

in the lungs; that is to say, it is a growth of fibroid tissue containing giant cells. I must disagree entirely with this. I have never seen in the lung of inoculated animals a true tubercle, that is to say, the reticular formation with giant cells, such as you will find in acute miliary tuberculosis of the tubercular form, and which, Payne says, is the essential type of the disease, and what we have always been taught to believe a tubercle. This fibroid tissue with giant cells you will not find in inoculated animals, therefore the disease does not reproduce itself in animals. I have been doing work lately in studying the changes produced by inoculation, where I could prove that the inoculating material was taken from pulmonary phthisis and pulmonary tuberculosis, and although I cannot speak positively, I believe that the result produced by inoculation of caseous products from pulmonary phthisis produces a condition similar to that in the lung of the inoculated animal; that is to say, the new condition is inflammatory, and goes on to breaking down. These are photographs of the lung of a monkey inoculated with pulmonary phthisis; there the change is exactly what you find in the inflammatory form of acute miliary tuberculosis; that is to say, there is no effect on the connective tissues of the lung, there is no attempt at new formation, and if this is the case it is a very important thing, because, on the other hand, inoculation with tubercular material has produced in the lung of a monkey an entirely new condition. This photograph is taken from the spleen, where the monkey was killed eleven days after the inoculation, and in the centre of the Malpighian corpuscle of the spleen is seen a mass of large cells, which are exactly similar to those found in a strumous cervical gland. You know in the

strumous cervical gland, which is one of the lymphatic glands, you have a number of masses of adenoid tissue, and between this physiological mass and capsule there is a lymph space forming a sinus there, the effect of the disease on one of these glands alters it entirely by the formation of these large cells, and the lymphatic tissue is entirely changed into masses of large cells with a number of giant cells in them with, after a time, caseation and breaking down in parts, which ends so often in suppuration. Now the effect produced in the monkey's spleen by the inoculation of tubercular matter has been to produce the formation of cells very similar to those found in struma or scrofula, there is certainly a strong resemblance, but as I have said, I have not had sufficient data as yet to speak positively on this. However, I am endeavoring to carry out the investigation, but I have to take the sputum from cases and inoculate guinea pigs, and trust to providence to give me a post-mortem, and I can't get one post-mortem in twenty, so I am wasting guinea pigs. But I would like to give you the idea, because it seems to me there must be something in this condition, but whether it will be ultimately proved that there is any connection between scrofula and this tubercular inoculation I can't say as yet.

The next point is as to the relation of the tubercle bacillus to the disease, and the proof of inoculation by pure culture of it in the production of tuberculosis. I don't think those who have worked in this have given any statements whatever as to what the products were; we have had the bald statement that histologically the lesion produced by inoculation was identical with that found in the lungs. And this has been stated by men who knew nothing whatever about normal histology. I have met it so often that

I feel convinced that such is the case, and I think it is materially hindering our investigations, especially in diseases of the lungs.

One other point I would like to mention is the consolidation produced in the lungs by other diseases. I have spoken so far of catarrhal pneumonia, caseation and the new formation tubercle, and then of the minor class of acute miliary tuberculosis which divides itself into two forms. But there are other conditions, lesions of syphilis and hydatids which sometimes are included in consolidations of the lungs. And another one is croupous pneumonia; we certainly sometimes get a consolidation produced by acute pneumonia remaining in the lung. While it remains in the lung as a solid mass it does not do much harm and gradually dries up, but it seems that some change will take place which produces an irritating action around the edge of the consolidated mass, and this may be either acute or chronic. If chronic, it does what chronic inflammatory action always does throughout the body, causes an increase in the fibrous tissue, and we know what the result is; we have the formation of fibrous bands of tissue in the lung caused by the chronic inflammatory action. But on the other hand, there may be an acute inflammatory process set up which results in the liquefaction of more or less of this consolidation, with the formation of a cavity from that, and here we have another way by which cavities are formed in the lung, and it certainly has no intimate relation with either inflammatory or acute tuberculosis. In regard to the clearing up of these different lesions in the lungs, we may, instead of having acute breaking down there and the formation of a cavity, have the mass dry up, and act as a chronic irritant in the lung, producing the usual

chronic inflammation, with the result that it is isolated by fibrous tissue ; and we have a chronic cystic tissue in the lung which will either leave a cicatrix there or else a fibrous capsule with a mass of caseous material in the centre.

With regard to those specimens, I cannot say what the condition originally was, the mass in the center is simply caseous, and whether it was a gumma or a tubercle, I cannot say. Whatever was there is broken down and all structure is lost, but still it has produced the same effect of setting up chronic inflammatory action.

I would ask if I were going to kill the tubercles, What would become of them? Do they remain in the lungs as foreign bodies and by their irritation set up these little fibrous cysts which contract on their contents? If so, it would seem to me that the last state of that man would be worse than the first, the remaining lung tissue would be put upon the stretch so that there would be a kind of mechanical emphysema produced which he could hardly sustain.

In regard to the argument in favor of tubercle bacillus being the virus of phthisis; if you make a pure cultivation of bacilli and keep cultivating that from one tube to another, extending over a number of years even,—it will not do to go too far or they will loose their vitality—you are supposed to free them entirely from anything which may have been introduced in the first place from the organ that they were taken from, and you are supposed then to have a pure culture, and that if you inoculate an animal with this it will produce a characteristic lesion. It will produce a change in the lung of the inoculated animal; this is a rather difficult thing to get over, because that, together with the histological consideration of the introduced lesion, are the main points on which

the position of the virus of tuberculosis rests. I would ask if it has been proved to demonstration that the cultivation of tubercle bacilli are absolutely pure? if nothing is carried from this mass on which they are cultivated? Has there been any attempt to prove that? That is a question which is very difficult to answer; but unless it is answered by exact science we may doubt it. We ought to consider all honest opinions, but we do not want to have opinions rammed down our throats as facts until they are proven. If this to be considered as the virus of the disease it must have its basis absolutely sure and certain before we accept it. Now take the example of the jequirity bacillus, which was found in an infusion of the beans sold in India as prayer beans. If you take an infusion of them and inoculate it into the eyes of animals you will produce an intense ophthalmia. It is used by the natives for trachoma, and produces an intense inflammation which lasts two or three days, and then all trace of the disease is gone. It has been found by investigation that after making this infusion and keeping it for two or three days, when it was examined it would be found teeming with bacilli. This bacillus was cultivated in the same way as tubercle bacillus. Generation after generation was cultivated by a man as careful as Sattler was known to be. Klein made these cultivations and worked it out thoroughly, and I recall his saying to me, "If there is any one case in which it is proved to demonstration that the bacillus is the virus of disease it is this." He made an infusion of the bean in sterilized water, with every precaution against contamination, and inoculated the eyes of eight rabbits, and eight tubes of sterilized peptones. He examined them every day for two or three weeks and not a trace of microörganisms grew in

them, but these animals got such an inflammation that they died with their heads swelled to an enormous size. He next took an infusion of jequirity bean teeming with bacilli and heated it to 100° centigrade and kept it so for a minute until the heat had destroyed all formed bacilli. He then took the spores from that and cultivated them until he grew bacilli morphologically identical with the bacillus he had before, but on inoculating the eyes of animals with it it had no effect whatever. Prof. Warden succeeded in isolating the alkaloid, not only from the beans, but the leaves, stems and root of the plant, and it was that which was doing all the mischief; it was shown beyond any doubt, in a case where it would seem to be absolutely proven that the bacillus was the virus of disease, that the bacillus had nothing to do with it.

Now I do not think we ought to take it as being absolutely true that the tubercle bacillus is the virus of the disease from the production of a lesion by an inoculation of so-called pure culture, and work on that line. Dr. Shurly and I have always held the view that there is something there beyond the bacillus, and we have never troubled the bacillus except to find when it has gone out in the sputum of the patient treated. We have not worried that bacillus at all, others have been doing that. We have been working on the line that there was some morbid product there which could be combined with some chemical and rendered inert. We commenced work with that idea, and we certainly did succeed by using iodine, and we got to that stage the year before last where we could inoculate a guinea pig with tuberculosis and prevent the development of it; prevent anything developing beyond an abscess at the seat of inoculation, where

we would find fluid pus full of bacilli, but with no lesions except fatty change in the liver, but which showed different conditions from ordinary fatty change, which, as you know, is generally around the periphery of the lobule. It was not necessarily confined to one lobule but sometimes running through the middle and changing into this fatty infiltration, so that when you held a section up you could pick out the patch that had undergone this change. We considered that we were not justified in doing this to human beings and we then turned our thoughts to other subjects. Dr. Shurly worked on animals while I worked on pure cultures of tubercle bacillus, until by using a number of things we found a way in which we could render the tubercle bacilli in the cultivation absolutely inert so far as the gross lesion in the guinea pig was concerned, although it was not dead. We considered we had done this by using some chemical which would combine with the morbid product which we thought, and still think, must exist in these cultures, and that we have rendered that innocuous by forming a combination of substances. The one I found most efficacious was chloride of gold and sodium. By using chloride of gold I killed the bacilli right off. I communicated with Dr. Shurly on the results and he was struck with the idea of injecting this substance. We had before been giving insufflations of different drugs, and he thought that by injection we could introduce this fluid in such a way as to be carried to these parts where the morbid product especially existed, and that it would act in the same way. We found we were justified in that by the effect on animals, and from that we went on trying the effect on human beings.

From what I have said I think you will see I

am at least justified in coming before such an assembly as this. I can assure you that it was with a great deal of trepidation that I began. I did not know whether I would be allowed to go on to the end. I have been sat down on so unmercifully on the other side that I feel considerably reduced in height in consequence. I hope you will not think I have been too dogmatic, but will pardon me when I say these conclusions are the result of careful work extending over eight or nine years. If you prove that I am wrong I hope you will let me down gently.